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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/848,820	05/19/2004	Timothy A. McKinsey	MYOG:044US/10405748	4787

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EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/848,820	MCKINSEY ET AL.	
	Examiner	Art Unit	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-11 and 100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-11 and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/28/2008 has been entered.

Claims 1 and 6-8 have been amended. Claim 5 has been canceled. Currently claims 1-4, 6-11 and 100 are pending.

Applicant is requested to note that the Examiner for this application has changed. Future correspondence should be directed to Laura Schuberg, Art Unit 1657, whose contact information can be found below.

Response to Arguments

Applicant's arguments filed 05/29/2008 have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or

newly applied. They constitute the complete set presently being applied to the instant application. Applicant's arguments have been addressed in so far as they relate to the new rejections below.

The rejection of claim 5 was inadvertently left out of the anticipation rejection under Dempsey in light of Wang and Matthews et al, therefore a new rejection has been made below including claim 5. Evidence providing support for the anticipation of claim 5, as well as other claims inadvertently left out, is cited in the rejection below.

Applicant's arguments regarding the obviousness rejection over Buchholz et al in view of Bing et al are not persuasive. Applicants have argued that it would not have been obvious to administer the combination, because one of ordinary skill in the art (i.e. Buchholz) was not expecting to treat cardiac hypertrophy. However cardiac hypertrophy is a symptom of hypertension. One would have inherently been treating cardiac hypertrophy regardless of whether the intent was to directly address a factor leading to hypertrophy, not hypertrophy itself. The outcome is the same. In addition the claimed invention does not require a specific level of hypertrophy only that hypertrophy or heart failure be treated. Furthermore, it is acknowledged that no citation reciting method steps explicitly states that protein kinase D is the intended target of staurosporine treatment, for example. Protein kinase D is a signaling factor that lies downstream of PKC. Because the cited references treat PKC with staurosporine, they inherently treat PKD activity. Intended consequences cannot be considered when considering whether method steps of prior art anticipate or make obvious method steps as instantly claimed. Because the steps are the same, the outcome must be the same. Furthermore, the

motivation need not be the motivation provided in the instant application, so long as some motivation exists to use the same drugs in humans as in a rat population. Bing teaches that humans with hypertension can be treated analogously to rats with hypertension and several of the references teach that hypertension in humans leads to cardiac hypertrophy in humans. Therefore, motivation exists to treat humans with staurosporine and beta blockers, regardless of whether the practitioner knew he was treating protein kinase D or not.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 9-11 and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Dempsey (US 6,228,843) in light of Wang (Trends Pharmacol Sci, June 2006) and Matthews et al (J Biol Chem, August 1997).

Claim 1 is drawn to a method of treating pathologic cardiac hypertrophy or heart failure in a human patient comprising: (a) identifying a human patient having cardiac hypertrophy or heart failure; (b) administering an inhibitor of PKD; and (c) administering a second cardiac hypertrophic therapy.

Dependent claims include wherein the inhibitor of PKD is selected from a group, the type of administration, wherein the second therapy is selected from a group, the timing of the second therapy, wherein treating comprises improving one or more symptoms of cardiac hypertrophy or heart failure.

Dempsey teaches a treatment method of treating cardiac hypertrophy and cardiac failure (column 14 lines 28-33). Treatment can comprise administering several drugs to inactivate protein kinase C. Specifically the drugs taught include bryostatin and Go6976 (see Fig. 4; see col. 3 line 62 to line 67, as examples). Wang teaches that PKD is phosphorylated by PKC. Dempsey teaches that his method functions by first activating PKC which then causes its degradation (see col. 11 lines 35-40, for example). Matthews et al teach that bryostatin activates PKD through PKC (see Abstract, for example); therefore it is inherent that administration of bryostatin causes degradation of PKC and inhibition of PKD signaling as taught by Dempsey. These drugs are effective in primates including humans, reading on the limitation that the patient is human (see col. 4, lines 1-6, for example). The drugs administered in combination with bryostatin include staurosporine, ACE-I (ACE inhibitors), and calcium channel blockers (Ca++-blocker) for example (see col. 12, lines 32-45, for example). They teach that the drugs can be administered in an oral or intravenous manner (see col. 6 lines 39-53, for example). Preferably the patient is treated by this method to an extent that the patient no longer suffers from the condition or wherein the discomfort and/or altered functions and detrimental conditions associated with the disease are decreased (column 9 lines

1-16). This is deemed to meet the limitation wherein the improved symptom is an increased quality of life.

Therefore the teachings of Dempsey are deemed to anticipate Applicant's invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-11 and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buchholz et al (Hypertension, 1991) in view of Bing et al (Heart Failure Rev, Jan 2002).

Buchholz et al teach a method of administering staurosporine to spontaneously hypertensive rats. Hypertension is known as a risk factor for hypertrophy, therefore selection of these rats reads on identifying a patient at risk of hypertrophy. Additionally spontaneously hypertrophic rats are well characterized as developing hypertrophy in response to their hypertensive disease (see Bing et al, 2002). They teach that one can administer staurosporine to rats intravenously and record arterial pressure and cardiovascular activity (see p. 93, col. 2, for example). They also administer staurosporine by gavage, reading on oral administration (see p. 93, col. 2, for example). They administer a second therapeutic, namely the beta blocker nadolol, to rats 5 min before intravenous administration of staurosporine. They teach that this combination lowers mean arterial pressure and decreases tachycardia (see Fig. 5, p. 97; see text, p. 95 last paragraph to p. 96, col. 1, as examples). The methods taught by Buchholz et al inherently have the results cited in claim 100. Regarding the limitation of claim 7 that administration of a beta blocker occurs simultaneously with staurosporine, it would be an obvious matter of convenience to the artisan whether to administer the drugs simultaneously or five min apart.

Bing et al teach that the spontaneously hypertensive rat is an ideal model for studying heart failure and hypertrophy as it applies to human disease (see Abstract, p. 71, col. 1, for example). They teach that it is normal practice to measure heart failure and heart improvement through measurements of cardiac output such as ejection fraction (see Introduction, p. 71, col. 2 for example). Additionally they teach that it is possible to measure changes in ejection fraction in spontaneously hypertensive rats approaching heart failure; they also teach that mortality is a useful parameter for measuring cardiac response to drug treatment (see "Prevention and Treatment of Heart Failure", p. 76, for example).

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer a PKD inhibitor such as staurosporine, alone or in combination with a beta blocker, to a human patient suffering from or suspected of suffering from cardiac hypertrophy or cardiac failure based on the combined teachings of Buchholz et al and Bing et al. One of ordinary skill in the art would have had a reasonable expectation of success in applying the method of Buchholz et al to humans because Bing et al teach that the spontaneously hypertensive rat is an ideal model for studying heart failure and hypertrophy as it applies to human disease (see Abstract, p. 71, col. 1, for example).

Therefore the combined teachings of Buchholz et al and Bing et al render obvious Applicant's invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg